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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,670	12/19/2005	Franco Macchi	207,380	5848

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EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,670	MACCHI, FRANCO	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 24, 2008 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed November 24, 2008, and amendment and response to the Final Office Action (mailed March 28, 2008), filed November 24, 2008 wherein claims 1, 10, and 11 are amended.

Claims 7-12 are pending and are examined on the merits herein.

The following rejections of record are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of recurrent oral aphthous ulcers and for reducing the occurrence of recurrent oral aphthous ulcers, does not reasonably provide enablement for the prevention of new recurrent oral aphthous ulcers. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a method for the treatment of oral cavity aphthas and for preventing the occurrence of new recurrent oral aphthous ulcers, comprising administering hyaluronic acid. No limiting definition of prevention is given in the specification. In the absence of a limiting definition by the applicant, the ordinary definition of prevent, "to keep from happening or arising; make impossible," is applied. The claimed composition capable of preventing the occurrence of new oral aphthous ulcers is therefore interpreted to one which is capable of eliminating the occurrence of new recurrent oral aphthous ulcers.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Nolan et al., enclosed as Annex 1 with Applicant's amendment submitted September 26, 2008, teaches a reduction of new ulcer occurrence in patients treated with HA compared to the placebo group [Table 4]. However, "new ulcers occurred throughout the investigation period." [page 463, second paragraph].

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the treatment of patients who have a current ulcer. However, the specification does not provide guidance for the prevention of ulcer formation. Patients who did not have a current ulcer were asked to contact the clinic at the onset of their next ulcer.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the teachings of Nolan et al. with respect to recurrence of

ulcers and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Response to Arguments

Applicant argues that the Nolan reference (Annex 1) provides evidence that HA can prevent or reduce new ulcer occurrence in patients affected by ROAU. Indeed, the reference shows that HA can reduce new ulcer occurrence, but HA cannot prevent new ulcer occurrence. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Schiena (EP 0444492, April 9, 1991, PTO-1449 submitted May 3, 2007) in view of Saxen et al. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 84:356-61, of record).

Di Schiena teaches pharmaceutical compositions comprising 0.2 to 10% sodium hyaluronate having molecular weight between 800,000-4,000,000, preferably

1,000,000-2,000,000 [page 2, line 52] for the treatment of inflammatory affections of the oral cavity [claims 1-10].

Di Schiena does not exemplify the treatment of recurrent oral aphthous ulcers using the composition.

Saxen et al. teach that recurrent aphthous ulcers are a common disorder, causing pain derived from inflammatory sensitization of nerve endings, and the most common treatment is topical anesthetics and topical steroids for pain management [page 356, first two paragraphs]. Adults having aphthous ulcers were treated with 3% diclofenac in 2.5% hyaluronan, 2.5% hyaluronan, or 3% viscous lidocaine. A reduction in pain was observed 10 minutes after application with no significant difference between the three topical agents [see abstract]. Ulcers were smaller after treatment with HA [page 359, Table 1]. The blunting action of hyaluronan may be due to the coating action over the ulcer [page 360, second full paragraph], and the protective layering of the ulcer was a significant component of the overall treatment effect [page 360, third full paragraph].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Di Schiena's composition for the treatment of recurrent aphthous ulcers. Di Schiena teaches that HA of molecular weight 1,000,000-2,000,000 is useful for treating inflammatory affections of the oral cavity, but does not specifically mention recurrent aphthous ulcers. Saxen teaches that HA alone can be used to treat recurrent aphthous ulcers, but is silent with respect to the molecular weight of the HA. The skilled artisan could expect that Di Schiena's composition would be useful for the

treatment of a specific inflammatory affection of the oral cavity, recurrent oral aphthous ulcers, because Saxen teaches that HA is effective for treatment of recurrent oral aphthous ulcers. The skilled artisan could expect that HA of molecular weight 1,000,000-2,000,000 could be effectively used in the method taught by Saxen because Di Schiena teaches that HA of that molecular weight is useful for treatment of inflammatory conditions of the mouth. Thus, the claimed invention is obvious over the prior art.

Response to Arguments

Applicant argues that ROAU has a pathology separate from other inflammations of the mouth and that the skilled artisan would not expect Di Schiena's teachings to be applicable to ROAU. This argument is not persuasive because HA is known to be effective for treating recurrent oral aphthous ulcers, as taught by Saxen.

Applicant argues that the molecular weight of HA used by Saxen is not disclosed, and that HA alone was less effective for long-term pain relief than HA with diclofenac, and that no significant change in ulcer diameter was observed. This argument is not persuasive because ulcers were smaller after treatment with HA [Table 1], and "a highly significant overall treatment effect" was observed in all groups [page 358, last paragraph]. Thus, the skilled artisan would know that application of HA to ulcers reduced pain and reduced the size of the ulcers somewhat.

Applicant argues that it is unexpected that HA as the sole agent would relieve pain and reduce the number of ulcers. This argument is not persuasive because Saxen teaches that HA treatment reduces pain and the size of ulcers. Saxen teaches that the

protective layering due to HA was a significant part of the therapeutic effect. Further, De Schiena teaches that HA of the specified molecular weight can be used for the treatment of inflammatory conditions of the oral cavity, which would include aphthous ulcers. Thus, it is not unexpected that HA as the sole agent would be effective.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/Layla Bland/
Examiner, Art Unit 1623